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10/720,091	11/25/2003	Sebastiano Cavallaro	17357.01202US	4892

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EXAMINER
EMCH, GREGORY S

ART UNIT	PAPER NUMBER
1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/720,091	CAVALLARO ET AL.	
	Examiner	Art Unit	
	Gregory S. Emch	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5-17,20 and 21* is/are pending in the application.

4a) Of the above claim(s) *1 and 5-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,20 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

Claims 1 and 3 have been amended, and claim 19 has been cancelled as requested in the amendment filed on 21 August 2008. Following the amendment, claims 1, 3, 5-17, 20 and 21 are pending in the instant application.

Claims 5-17 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected subject matter, there being no allowable generic or linking claim. Additionally, newly amended claim 1 is withdrawn from consideration as no longer encompassing the elected invention. In the reply filed on 14 August 2006, Applicants elected Group I, drawn to a method of enhancing learning, memory and or attentive cognition in an individual, comprising administering an effective amount of FGF-18 and Species A, drawn to impaired cognitive performance for examination. Thus, since claim 1 is now directed a method "wherein the human subject does not have an impairment in memory, attentive cognition or learning" said claim is now drawn to subject matter that is not encompassed by the elected species. Thus, claim 1 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 3, 20 and 21 are under examination in the instant office action.

Withdrawn rejections

The rejection of claim 1 under 35 U.S.C. 103(a) as being unpatentable over Ellsworth et al. in view of US 2001/0039261 to Finklestein is withdrawn in response to the amendment of said claim.

The rejection of claim 19 under 35 U.S.C. 103(a) as being unpatentable over Ellsworth et al. in view of US 2001/0039261 to Finklestein is withdrawn as moot in response to the cancellation of said claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The rejection of claims 3, 20 and 21 under 35 U.S.C. 103(a) as being unpatentable over Ellsworth et al. in view of US 2001/0039261 to Finklestein is maintained for reasons of record and as set forth below.

In the reply filed on 21 August 2008, Applicants assert that Ellsworth et al. do not teach that FGF-18 can enhance memory, attentive cognition or learning in an animal or human subject who has not been subjected to/afflicted with cerebral ischemia, i.e. with no impairment. Applicants assert that Finkelstein does not remedy this deficiency because the reference is also limited to using bFGF to treat neuronal damage resulting from cerebral ischemia, i.e., stroke. Applicants assert that Finkelstein teaches only that use of bFGF improves post-ischemic sensorimotor deficits as evidenced by the fact that none of the functional tests disclosed by Finkelstein are designed to evaluate memory, cognition, or learning, but are designed to measure sensory or motor defects. Accordingly, Applicants assert that one of ordinary skill in the art seeking to enhance

memory, attentive cognition, and/or learning would not have looked to Finkelstein for guidance.

Applicants' arguments have been fully considered and are not found persuasive. The Examiner agrees that Ellsworth et al. do not teach that FGF-18 can enhance memory in a subject with no deficit. Note that the rejection of claim 1 has been withdrawn. Regarding Applicants' argument that the skilled artisan would not be motivated to combine the disclosure of Finkelstein with that of Ellsworth et al., it is noted that KSR forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. See the recent Board decision *Ex parte Smith*, --USPQ2d--, slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing KSR, 82 USPQ2d at 1396) (available at <http://www.uspto.gov/web/offices/dcom/bpai/prec/fd071925.pdf>). Rather, the rationale for the instant finding of obviousness is that the claims would have been obvious because a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. As evidenced by the prior art, the skilled artisan would have known that human patients can be treated with an FGF family member to enhance cognitive performance (as taught by Finklestein) and that FGF-18 can be used in such methods (as taught by Ellsworth et al.). Furthermore, it would have been reasonable to predict that humans could be successfully treated with FGF-18. Thus, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to improve Ellsworth et al.'s treatment methods in rats by practicing the invention in human subjects as taught by Finklestein et al. and as expressly

suggested by Ellsworth et al. Such would amount to a substitution of known equivalents to yield predictable results. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense.

In the reply filed on 21 August 2008, Applicants assert that neither Ellsworth et al. nor Finkelstein disclose using any FGF to ameliorate impaired cognitive performance associated with impaired function of the hippocampus. Applicants further submit that neuronal damage to the hippocampus is not necessarily implicated in models of cerebral ischemia disclosed in Ellsworth et al. and Finkelstein. Applicants assert that both Ellsworth et al. and Finkelstein disclose induction of cerebral ischemia by occlusion of the middle cerebral artery and that this model is commonly used when damage to the frontal and parietal areas of the cortex is sought. Applicants assert that typical impairment resulting from middle cerebral artery occlusion (MCAo) includes weakness and sensory loss in the extremities and lower face, aphasia (impaired speech), hemineglect (lack of awareness of items to one side of space), lateral gaze weakness, and visual loss. Applicants assert that to induce ischemic neuronal damage to the hippocampus, occlusion of the carotid arteries is performed. Applicants assert that even carotid artery occlusion will not necessarily impair the hippocampus in every instance under every circumstance. Applicants assert that the areas of the cortex that are damaged by MCAo adversely affect both reference and working memory and that the prefrontal cortex is well-known to be implicated in working memory (short term). Applicants assert that other areas of the brain, including the parietal cortex, perhinal cortex, and anterior cingulated cortex are involved in reference memory. Applicants

assert that damage to areas of the cortex, such as those damaged in the ischemic models taught by the prior art, can adversely impact both working reference memory. Applicants assert that the hippocampus is not within the cortex and that because neither Ellsworth et al. nor Finkelstein teach or suggest that the deficits resulting from cerebral ischemia are caused by impairment of the hippocampus, and because the model used by both is not a model used to evaluate injury to the hippocampus, the references alone or in combination do not render claims 3, 20 and 21 obvious. Applicants assert that the ischemic stroke model used by Ellsworth et al. would not necessarily impair the hippocampus.

Applicants' arguments have been fully considered and are not found persuasive. Contrary to Applicants' arguments, the Ellsworth et al. abstract discloses administration of FGF-18 to ameliorate impaired cognitive performance, "wherein the impaired cognitive performance is associated with impaired function of the hippocampus," as evidenced by Ellsworth et al. (Fibroblast growth factor-18 reduced infarct volumes and behavioral deficits after transient occlusion of the middle cerebral artery in rats. Stroke. 2003 Jun;34(6):1507-12) and Corbett et al. (The problem of assessing effective neuroprotection in experimental cerebral ischemia. Prog Neurobiol. 1998 Apr;54(5):531-48). The Ellsworth et al. (2003) reference is the full journal article that discloses the entire experimental protocols that were performed in the Ellsworth et al. abstract (of record, primary reference for the instant rejection under 35 U.S.C. 103 (a)). It is noted that claim 3 and its dependent claims do not absolutely require that the hippocampus is damaged, per se. Rather, claim 3 requires that the impaired cognitive performance that

is treated in the subject "is associated with impaired function of the hippocampus." Indeed, the cognitive performance treated by FGF-18 as disclosed by Ellsworth et al. is associated with impaired function of the hippocampus. The Ellsworth et al. abstract and journal article both teaches that intravenous infusion of FGF-18 decreased deficits in reference and working memory, exploratory behavior and motor activity in rats with impaired cognitive performance after middle cerebral artery occlusion (thus enhancing memory, attentive cognition or learning, as in claims 3, 20 and 21). The Ellsworth et al. journal article teaches that the impaired cognitive performance that was treated in the Ellsworth et al. abstract was measured by testing of rats in the Morris water maze (p.1508, col.1, paragraph 2). Accordingly, the water maze test is a behavioral test used in examining impaired function of the hippocampus (see Corbett et al. p.535, under 4.2. Rat Behavioral Studies). Here, it is taught that the behavioral tests sensitive to hippocampal injury are also sensitive for detecting global ischemic injury, such as the Morris water maze test. Indeed the instant specification also teaches that the Morris water maze "is a widely accepted method of measuring hippocampal learning and memory performance" (see specification at p.3, [0009], first sentence). Thus, since this test is associated with impaired function of the hippocampus and since this test was used to measure the impaired cognitive performance in the Ellsworth et al. abstract, the impaired cognitive function that was treated in the Ellsworth et al. abstract is indeed associated with impaired function of the hippocampus. Therefore, the rejection is properly maintained.

Conclusion

No claims are allowed.

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory S. Emch whose telephone number is (571) 272-8149. The examiner can normally be reached 9:00 am - 5:30 pm EST (M-F).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey J. Stucker can be reached at (571) 272-0911. The fax phone

number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/G.E./

Gregory S. Emch, Ph.D.
Patent Examiner
Art Unit 1649
05 December 2008

/Jeffrey Stucker/
Supervisory Patent Examiner, Art Unit 1649